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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/821,545

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Michael E. Hepperle

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08/29/2008

MILLENNIUM PHARMACEUTICALS, INC.

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CAMBRIDGE, MA 02139

EXAMINER

BIANCHI, KRISTIN A

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

08/29/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/821,545	Applicant(s) HEPPERLE ET AL.	
	Examiner KRISTIN BIANCHI	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,9,17,28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 28 and 29 is/are allowed.
- 6) ☒ Claim(s) 1,9 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/30/2006 and 11/26/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 9, 17, 28, and 29 are pending in the instant application. Claims 28 and 29 appear allowable. Claims 1, 9 and 17 are rejected.

Response to Amendment

Applicants' amendment and arguments filed on July 9, 2008 have been considered and entered into the application. Applicants' amendment has overcome the claim objection of claim 1 and the 35 USC 112 2nd rejection of claims 1, 9 and 17. While applicant has stated that the provisional nonstatutory obviousness-type double patenting rejection of claims 1, 9 and 17 will be addressed when allowable subject matter is indicated, it is noted that as the provisional rejection is considered proper, therefore, it is maintained. The 35 USC 103(a) rejection of claims 1, 9 and 17 is also maintained.

In regards to the 35 USC 103(a) rejection of claims 1, 9 and 17, Applicants argue that there is no suggestion or motivation in Castro *et al.*, alone or *combined with knowledge generally available in the art*, to modify the reference to arrive at the claimed invention, nor does it provide any reasonable expectation that modification of the morpholine ring to include methyl would successfully yield compounds having activity against IKK that would be useful for the disease or disorders described by the Applicants. Applicants also argue that a *prima facie* case of obviousness also requires a showing of adequate support in the prior art for the change in structure. These arguments are not persuasive because the motivation to make the claimed compounds derives from the expectation, which is known in the art and was at the time of the

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invention, that structurally similar compounds possess similar properties and, therefore, similar activities (i.e. the compounds disclosed in Castro *et al.* are used for the same purpose or have the same activity as the compounds disclosed in the instant application, as inhibitors of IKK). To those skilled in the chemical art, one homologue is not an advance over an adjacent member of a homologous series. One of ordinary skill, knowing the properties of one member of a series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950), In re Wood, 199 USPQ 137 (CCPA 1978) and In re Lohr, 137 USPQ 548, 549 (CCPA 1963). The reasonable expectation of success derives from the fact that it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. There would also be a reasonable expectation of success for the reason stated above (i.e. structurally similar compounds possess similar properties and, therefore, similar activities). As stated in the MPEP § 2144.08 (4. II A. (d)) “In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) (“When chemical compounds have very close structural similarities and similar utilities, without more a prima facie case may be made.”). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972)”. Applicant also argues that when considered as a whole, Castro *et al.* teaches

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away from the use of the morpholine substituent because compound 35 has a higher IC50 value than the compounds that do not have morpholine as a substituent. This argument is not found to be persuasive because even though the morpholine substituted compound 35 has a higher IC50 value than the non-morpholine substituted versions, it still does, in fact, inhibit IKK. Therefore, the fact that it inhibits IKK would provide enough motivation to make additional morpholine substituted compounds to test out their activity against IKK. For all the reasons stated above, the Examiner has established a *prima facie* case of obviousness and the rejection is maintained.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/461,468 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, claims 1, 9, 17,

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28 and 29 are not entitled to the benefit of the prior application as subject matter found in the instant claims does not find support in Application No. 60/461,468. For example, wherein Ring A is a morpholinyl that is substituted by (i), (ii) and (iii) does not find support in the prior-filed application as the prior-filed application only provides support for morpholinyl attached at the 3-position with specific substituents. Additionally, wherein R1 is halo and R3 is cyano also does not find support in the prior-filed application as the prior-filed application does not allow or provide a definition for R1 and R3 as halo or cyano, respectively.

Accordingly, claims 1, 9, 17, 28 and 29 are not entitled to the benefit of the prior application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9 and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 10, 15, 16, 19, 28 and 29 of copending Application No. 11/101,998. Although the conflicting claims are not identical, they are not patentably distinct from each other because conflicting claims 3, 10, 15, 16, 19, 28 and 29 provide compounds and pharmaceutical compositions which overlap with applicants instantly claimed elected invention. Conflicting claim 3 provide products which overlap with applicants' instantly claimed elected invention. Conflicting claims 10, 15 and 16 provide preferences towards applicants' instantly claimed elected invention such as wherein the compound is (S) (claim 10); wherein G is N-piperidinyl, N-piperazinyl, N-morpholinyl or N-pyrrolidinyl (conflicting claim 15); and wherein Rb is methyl (conflicting claim 16). Conflicting claim 19 provides pharmaceutical compositions. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castro et al. (C1 reference on 1449 and U reference on 892).

Determining the scope and contents of the prior art

Castro et al. discloses the compound 35 and registry no. 590398-98-4 useful to inhibit IKK for the treatment of certain inflammatory diseases (pages 2419 and 2421 and abstract).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art provides an unsubstituted ring A wherein ring A of the instant claims is substituted by at least one of C(R₉)₃, W-G or G, wherein C(R₉)₃ can be methyl. Therefore, the difference between the instant claims and the prior art can be a hydrogen versus a methyl on the morpholine ring.

Resolving the level or ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare compounds of applicants instant elected invention when faced with the prior art of Castro et al., which discloses compound 35 and registry no. 590398-98-4 which are useful as inhibitors of IKK for the treatment of certain inflammatory diseases. It is well established that the

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substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e., inhibitors of IKK).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIN BIANCHI whose telephone number is (571)270-5232. The examiner can normally be reached on Mon-Fri 7am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed, Ph.D./
Primary Examiner, Art Unit 1626

Kristin Bianchi
Examiner
Art Unit 1626

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